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Refractive surgery to visually rehabilitate refractive errors of the eye continues to evolve at a signficant pace and is here to stay. The surgical manipulation of the cornea by carefully planned incisions, as in radial keratotomy, represented the first technological procedure to evolve for the correction of ametropia and is an area of continued active development and improvement. More recently, photorefractive keratectomy (PRK) using laser technology to ablate and recontour the corneal surface has emerged as a viable modality. This paper explores the aeromedical factors surrounding this new revolutionary procedure and discusses the issues relevant to evaluating its applicability to the modern aviator as well as reviewing results of the latest clinical trials currently in progress. The goal is to provide the aeromedical community with the fundamental information required to formulate aeromedical decision- and policy-making in regard to a new procedure that is certain to have tremendous impact on future aircrew candidates.

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PHOTOREFRACTIVE KERATECTOMY (PRK) IN THE MILITARY AVIATOR: AN AEROMEDICAL EXPOSE

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SUMMARY

Refractive surgery to visually rehabilitate refractive errors of the eye continues to evolve at a significant pace and is here to stay. The surgical manipulation of the cornea by carefully planned incisions, as in radial keratotomy, represented the first technological procedure to evolve for the correction of ametropia and is an area of continued active development and improvement. More recently, photorefractive keratectomy (PRK) using laser technology to ablate and recontour the corneal surface has emerged as a viable modality. This paper explores the aeromedical factors surrounding this new revolutionary procedure and discusses the issues relevant to evaluating its applicability to the modern aviator as well as reviewing results of the latest clinical trials currently in progress. The goal is to provide the aeromedical community with the fundamental information required to formulate aeromedical decision- and policy-making in regard to a new procedure that is certain to have tremendous impact on future aircrew candidates.

LIST OF ACRONYMS

PRK	photorefractive keratectomy
RK	radial keratotomy
UV	ultraviolet radiation
UVC	short wavelength UV less than 300 nm
nm	nanometer
D	diopters of refractive power
eV	electron volts
VA	visual acuity
BVA	best (corrected) visual acuity
IOL	Intraocular lens

I. INTRODUCTION

Surgical intervention to alter the optical refractive state of the eye is known as refractive surgery. Current procedures have evolved in an attempt to permanently correct myopia (nearsightedness) and, to a lesser extent, in less commonly expressed refractive problems such as excessive astigmatism and hyperopia (farsightedness). Universal acceptance of such a procedure will depend on its success, predictability, stability and safety. A listing of applied surgical techniques to date is as follows:

A. Radial keratotomy (RK)
   1. Hand-made incisions (RK)
   2. Laser incisions (LRK)
B. Epikeratophakia (EPI)
C. Thermokeratoplasty (TK)
D. Laser thermokeratoplasty (LTK)
E. Myopic keratomileusis (MKM)
   1. Manual
   2. Automated lamellar keratoplasty or keratomileusis (ALK)
F. Laser ablation
   1. Corneal surface ablation - PRK with or without erodible mask

2. Intrastromal ablation (ISA)

G. Myopic intraocular lenses (MIOL)

H. Synthetic corneal inlays

I. Laser-adjustable synthetic epikeratophakia (LASE)

Each of these procedures will be described briefly to enhance our background understanding and to differentiate them from the subject of this expose, PRK. Unquestionably, the evolution and application of laser energy to alter the shape of the eye is an exciting and promising technological development of major significance to medical science and the "war" on myopia. Corneal surface ablation that alters the shape of the cornea using excimer laser technology (PRK) currently represents the most common laser procedure to evolve--one that has attracted considerable international attention, and with it the hopes of ophthalmic surgeons and many myopes.

<u>Refractive Surgical Procedures</u>

Radial keratotomy (RK): In this procedure, the surgeon makes between 4 and 16 radial incisions extending through 90% of the corneal thickness and running from the edge of the optical zone to the corneal periphery (limbus) to flatten the corneal surface. These incisions can be made either by a surgical knife or, more recently, by a surgical laser. Considerable international experience has accumulated with standard, hand-made RK; the laser variant appears to be less optimal. RK has been practiced for a number of years, and although it continues to evolve technologically, it may have reached its clinical zenith. It remains a popular surgical procedure to myopes despite some potential drawbacks.

Epikeratophakia (EPI): This procedure involves the removal of a portion of the central cornea, which is discarded and replaced with a specially contoured implant, made from either a donor cornea or synthetic materials. EPI has limited application; it is primarily used for the optical correction of high degrees of hyperopia such as in aphakia (post-cataract surgery). It is a specialized procedure, performed by a small number of surgeons in a very limited number of cases.

Thermokeratoplasty (TK/LTK): The application of heat to the corneal surface to induce a change in corneal contour, can be achieved with cautery probes or using laser energy (i.e., infrared HOLMIUM laser). It has been used primarily in hyperopia, and although manual application procedures have waned, there is a current resurgence of this technique, rekindled by new applied laser technology.

Myopic keratomileusis (MKM): In this procedure, also referred to as epikeratoplasty, a portion of the central cornea is removed and frozen, lathe cut to recontour, then sutured back onto the original site, resulting in an altered corneal curvature and a new refractive power in the cornea. Recent developments, including enhanced control by microtome automation, are being investigated in a new procedure known as automated lamellar keratoplasty (ALK). This is a complex procedure; in its present form, ALK has limited application, unless techniques evolve to permit greater universality. At present, it is used for high degrees of myopia (up to -30 D), with limited application in the general population of myopes.

Myopic intraocular lenses (MIOL): In this procedure, a myopic anterior chamber IOL is implanted to correct preexisting myopia. It is a relatively new, evolving intraocular surgical procedure with limited clinical experience and application.

Synthetic corneal inlays: In the synthetic corneal inlay procedure, an intrastromal corneal ring made of polysulfone or hydrogel is implanted to alter the anterior corneal curvature. It's a new procedure, currently under technical development.

Laser-adjustable synthetic epikeratophakia (LASE): This procedure employs a collagen exoplant previously sculpted by laser energy to a desired shape and power and attached to the eye. It is a new procedure and has had limited studies to date.

Laser Intrastromal ablation (ISA): In ISA, laser energy is applied directly to corneal stromal tissue. Theoretically, its premise is to collapse or flatten the corneal surface by selectively destroying deeper portions of the underlying supporting corneal stroma, to avoid potential problems associated with removing superficial corneal layers. ISA is an emerging procedure with technical merit and potential universal applications.

Laser surface ablation (PRK): In this procedure, the surgeon uses laser energy to create a central corneal plateau or flattening that reduces the plus refractive power of the cornea. Representing, overwhelmingly, the most common form of laser ablative surgery to date, PRK is considerably advanced in its clinical application internationally; it is the focus of this paper.

II. PRK

In PRK, the ophthalmic surgeon uses the excimer laser to alter (flatten) the corneal contour. It employs 193 nm UVC light, emitted from an excited dimer ("exc-imer") of argon fluoride (ArF). Selection of this wavelength was based on intended effect, predictability, associated complications, and the impact on surrounding corneal tissue. PRK has been used in both human and animal studies since 1986, with an estimated 70,000 human procedures already performed using systems made by 5 manufacturers. The procedure depends on the photoablative effects of high-energy UVC which causes ultrafast vaporization of the cornea by direct photochemical disruption of molecular bonds from photic, photothermal and photomechanical mechanisms. Two laws of physics applicable to PRK are the Grotthus-Draper Law, which states that light must be absorbed by a molecule before a photochemical effect can occur, and the Stark-Einstein Law, which states that the absorption of only one photon is required to affect one molecule. Infrared radiation induces molecular rotational and vibrational changes and is associated with voltages in the 0.01-1.0 eV range. UV and visible wavelengths are associated with higher energy and induce electron changes that involve excitation of valence electrons at levels below 3.0 eV, chemical bond breakage in ranges of 3.0-6.0 eV, or complete ionization and bond breakage at energy levels greater than 6.0 eV. UVC energy levels (6.4 eV) used by the excimer laser result in the removal (vaporization) of a central zone of corneal tissue with, theoretically, minimal or acceptable impact on the surrounding ocular structures.

However, a byproduct of this type of tissue interaction is the production of free radicals. The corneal layers removed by this procedure include the corneal epithelium, basement membrane, Bowman's layer and portions of the corneal stroma. The amount of tissue removed is dependent upon the initial refractive status of the patient and the desired optical result. Upwards of 10% (e.g., a -5.00 D myope) of the cornea may be removed. The surgery is intended to produce a flattened corneal plateau, thus reducing the overall plus refractive power of the cornea and subsequently the amount of minus power required for optical correction. The procedure is targeted primarily at -2.00 D to -7.00 D myopes. To be clinically acceptable, treated corneas should be clear, smooth, predictably contoured, and stable following the procedure. The development of an erodible mask, used in conjunction with the application of the excimer laser, broadens the scope of this procedure, to include both astigmatism and hyperopia. This mask is composed of polymethyl methacrylate (PMMA), which absorbs UVC and is eroded (vaporized) in the process, and a quartz substrate, which transmits UVC without destruction. The surgeon uses these specifically contoured masks to control exactly where and how the laser energy is applied to the cornea, thus allowing selectively contoured corneal surfaces beyond the limitation of an unmasked laser-determined central plateau.

PRK Procedure

Clinically, the procedure can easily be perceived to be oversimplified. The corneal epithelium may or may not be removed prior to the application of the laser energy. After programming the amount of intended refractive change required and baseline ophthalmologic examination data, an algorithm determines the desired excimer treatment parameters. Using helium-neon (HeNe) aiming beams, the patient is directed to look into the aiming device while the surgeon positions the patient's head manually for the procedure. Laser energy is then applied typically over 20-40 seconds, during which time the corneal surface is almost "magically" and irreversibly altered. Postoperatively, the eye is patched for a few days to promote reepithelialization and healing; topical steroids are employed to control postoperative changes. Postoperative care involves management of the reepithelialization process and steroid-dependent factors such as refractive outcome, anterior stromal haze and steroid-induced rises in intraocular pressure. The recent trend is toward reducing steroid use, substituting non-steroidal anti-inflammatories, and for shorter periods of time, approximately 3 months. However, steroids seem more efficacious, minimizing post-PRK inflammation and corneal haze, and playing a role in preventing postoperative regression (1,2,3). Clinically, their use seems unavoidable.

Demographics

U.S. demographic studies (4) predict that by the year 2000, approximately 8 million PRK procedures will have been performed in the U.S. at a rate of 3.5 million per annum. International projections in combination portend of a tremendous pool of applicable PRK candidates who will pursue this procedure enthusiastically.

There is no question that PRK will appeal to most myopes and offers some significant advantages over RK. The most important advantages are the reduction in the risks from intraocular penetration during surgery, less refraction instability, and the retention of near-normal corneal rigidity, severely compromised with RK. The collective international experience (nearly 40 countries) with PRK is 7 years old and involves nearly 70,000 patients, while the U.S. experience is less than 3 years old and involves approximately 3,000 patients. The procedure currently costs approximately $2,000 U.S. per eye and approximately $300,000 U.S. for the excimer laser. However, even pessimistic demographic estimates still encourage medical and commercial development.

Postoperative Results

A review of the literature and data from a current user group symposium reveals that PRK, even early in its technological development, is currently about equal to RK in terms of VA results. Most groups performing PRK report postoperative vision is 20/20 or better in 58-75% of eyes and 20/40 or better in 85-95% of eyes at 1 year. Depending on the preoperative amount of myopia, the percentage of postoperative refractive errors achieved short-term within $\pm$1.00 D of emmetropia (plano) ranges from 70% to 98% in myopes with preoperative refractions less than -3.00 D, from 60% to 92% in myopes between -3.00 and -6.00 D, and from 35% to 44% in myopes between -6.00 and -9.00 D (5,6,7,8,9,10). Even with relatively short periods of follow-up, PRK compares favorably to RK. It can be expected that, as PRK techniques continue to evolve, postoperative results are likely to improve; exactly to what final level, only time will tell. Factors such as the use of erodible masks, new technology, aperture size, control of energy emission profiles, postoperative management, and improved programming algorithms are likely to achieve improved risk/benefit ratios. This outlook presumes no catastrophic issues arise. Until recently, it has been generally recognized that it usually takes approximately 1 year for the refraction to stabilize post-PRK, and this period may even be longer in higher myopes (1,8,11,12,13).

Complications

The main potentially significant issues associated with PRK so far include:

Corneal scarring
Haze/glare/starbursts
Pain
Instability of refraction
Loss of best correctable VA
Recurrent erosions
Over/under correction
Topical steroid complications
Decentration
Corneal islands
UVC exposure

Corneal scarring/haze/glare/starbursts/haloes: Corneal scarring, in the form of corneal haze, is present in virtually all patients postoperatively, fades invariably, and is subject to individualized interpretation and significance. There is no question that the haze occurs and seems to peak in 3-6 months. It is a result of inflammatory and induced histological changes. Analysis of human specimens has been limited, but animal studies and some human specimens have revealed epithelial hyperplasia, increased fibroplastic activity, absence of Bowman's layer, and, following initial obliteration,

reformation of an often discontinuing basement membrane (14, 15,16,17). There has been some evidence of induced Descemet's membrane changes and electron-dense granular material has been seen in primate studies (14) and identified as Type III collagen material, normally not part of the corneal histology (16). These histological changes frost the corneal optical window and are believed to be the source of postop visual haze, glare and starbursts and a factor in causing haloes. Our ability to evaluate the impact of haze and glare objectively and, more specifically, aeromedically is not ideal. In general, all patients will have readily observable corneal haze for 3-6 months postoperatively and most experience significant fading by 1 year (8,9,18). The greater the intended refractive change, the greater and more persistent the corneal haze, which parallels the poorer post-PRK VA results associated with higher myopes. One primate study revealed the histological changes believed to be responsible for corneal haze to persist when the animals were sacrificed at 18 months (16). Corneal clarity postoperatively impacts on several aspects of visual performance, especially at reduced light levels and at night.

Pain: All patients experience pain post-PRK because of removal of the corneal epithelium. This pain generally resolves with reepithelialization of the cornea, which occurs 3-5 days postoperatively. Although corneal pain may have a rate-limiting effect on some individual decisions whether to have the procedure, it is not considered an unmanageable or prolonged problem.

Instability of refraction: By design and from clinical experience, most patients are overcorrected during the first month following PRK and regress over the next 3-6 months. Based on short-term follow-up, it had generally been accepted that the refraction remains unstable for up to 1 year postoperatively, settling within $\pm$1.00 diopter of emmetropia 75-98% of the time. It is associated with 20/20 vision or better in 58-75% and 20/40 or better up to 95% of the time in myopes less than -3.00 D preoperatively (5,6,7,8,9,10). Individuals with higher preoperative refractions have poorer results in general. However, recent observations of late regression beyond 18 months and up to 26 months post-PRK have raised clinical concern that stromal healing may be much slower than had previously been assumed. Persistence of what appears to be the original concentric ablation rings beneath the epithelium has seriously challenged the stromal remodeling hypothesis in post-PRK healing (19). Residual refractive errors occur at least 40% of the time and in most cases would require postoperative correction of some type to achieve best corrected visual acuity (BVA).

Recurrent erosions: Postoperatively, the corneal epithelium must reattach to the underlying corneal stroma. Normal histology involves the reattachment of the epithelium to the underlying basement membrane and Bowman's layer. However, in this procedure, the natural Bowman's layer and basement membrane are deliberately removed; consequently, the corneal epithelium must reestablish anchoring fibers to underlying corneal stroma and reconstituted basement membrane. Basement membrane material is reproduced similar histologically to the original

in most aspects, but differs to some degree. Bowman's layer is not reconstituted, but no one fully understands the importance of this layer to the cornea. Although reepithelialization occurs in all patients within the first postoperative week, the long-term potential for recurrent erosions, especially when these eyes are challenged with contact lenses, remains undetermined. However, most groups have reported that recurrent erosions are not a significant problem short-term. Recent reports of recurrent erosions have emerged and preclude us from totally ignoring this possibility. No post-PRK contact lens studies have yet been reported.

Over/undercorrection: Undercorrection of refractive error can either be an intended surgical target or a result of stromal healing/epithelial hyperplasia. Although most cases are deliberately overcorrected postoperatively, these changes tend to regress over the next 3-6 months. Some investigators have reported changes beyond the 12-month period, so far as late as 26 months, but generally at least 1 year usually has been necessary for stability. Residual undercorrection could potentially be retreated with an additional PRK. However, once corneal tissue is removed and a residual overcorrection exists, correction will require the use of glasses, contacts, or more extensive surgical intervention such as corneal transplantation, or perhaps future laser application. Large overcorrections remain one of the most serious complications and have been reported to occur more often in steroid responders (20).

Long-term topical steroid use: All patients require the use of topical steroids to minimize the corneal haze noted postoperatively and appear to undergo myopic regression if steroids are discontinued too soon (3,21,22,29). However, steroids secondarily delay normal healing, and abrupt cessation of topical steroids has been associated with dense corneal scar formation. To a certain extent, utilization of this medication is dependent upon postoperative response. Some patients may require more prolonged steroid treatment than others. A recent double-blind study supports no statistical significance associated with either anterior stromal haze or refractive outcome after 6 months following PRK, with or without steroids (2), but others dispute this finding (3,21,22). A significant rise in intraocular pressures, associated with long-term steroid use (greater than 3 weeks), has been reported in 11-24% of cases (8). Because of these issues, topical nonsteroidal anti-inflammatory agents are being investigated, but ultimately may not be found as effective in reducing corneal haze as steroids. Clinical experience with respect to this issue continues to evolve.

Decentration: It is important that the photoablated zone be reasonably centered around the visual axis. However, one of the most disastrous consequences is eccentric ablation or decentration in the application of the laser energy. This phenomenon is associated with the most serious postoperative subjective complaints, increased postoperative astigmatism, and the greatest loss of BVA. It has been associated early on with 5% of cases using the erodible masks (20). Although it's rare, when it occurs, it presents a difficult challenge and may ultimately

lead to penetrating keratoplasty (corneal transplant).

Decreased BVA: The potential to permanently reduce BVA postoperatively has been recognized as a problem following PRK. Philosophically, surgeons define success, VA, and scarring differently following PRK. The factors that determine postoperative VA are basically a combination of histological corneal changes, scarring, related optical factors, and a reduction of contrast sensitivity. Regardless, permanent loss of BVA of one or more lines after 2 years has been reported to be as high as 8% of cases in myopes with less than -7.00 D preoperatively and 12-18% in individuals greater than -7.00 D (8,11). It is important to realize that this has been for the duration of follow-up, which has been as much as 2 years in the cited studies. Improvement with time remains a possibility.

Corneal islands: One of the optical requirements of any corneal sculpting procedure is that the resultant refracting surface, in this case the anterior corneal surface and the reepithelialization process, must be smooth and clear. One area of technical evolution in PRK has been directed at controlling how the laser energy is applied to the cornea to smooth the transition from normal cornea to ablated cornea. So far, the histological response to uniform applied energy has had some inherent unpredictability and uncontrollability. In general, the better the transference of the energy and control of its impact on the cornea, the better the post-PRK refractive surface that remains. One issue concerns irregular surface impact of the laser secondary to poor homogeneity in the beam profile. This problem may be exacerbated by other elements such as optical changes in the mirrors or optics of the system and local tissue effects from plasma shielding (23). Second- and third-generation excimer lasers (i.e., the mini-excimer) are being designed to improve upon the laser energy profile and to reduce the potential for surface irregularities from homogeneity of the beam. These factors, in combination with enhanced algorithms, will most certainly improve upon this aspect of the procedure, but it's too early to tell to what extent.

UVC exposure: The excimer uses 193 nm UVC energy. This wavelength possesses sufficient energy levels (6.4 eV) to break biological and chemical bonds, resulting in the formation of free radical byproducts in the surrounding tissue. The mutagenic and carcinogenic potential from this process is difficult to assess. However, the association with the production of free radicals from these types of energy levels and tumorigenesis and cataracts has been established. The human cornea concentrates free radical fighters such as glutathione and vitamin C in the anterior stroma, presumably to counteract this phenomenon from ambient UVA and UVB exposure. Nonetheless, there is a higher association of cataracts with chronic sun exposure. Whether these free radical fighters are sufficient to counteract the effect of the more destructive UVC wavelengths long-term is unknown.

III. AEROMEDICAL ISSUES

The formula for success following this procedure is variable, dependent on both objective and subjective criteria. Surgeons might define success as a function of the final VA achieved

and its complications. Patients, on the other hand, may define the success of this procedure as the ability to exist without the encumbrances of thick glasses. Their new visual status, even though it may be associated with some subjective complaints, may be well tolerated, given the alternative. On the other hand, when we approach surgical procedures aeromedically, these perceived minor annoyances in the general population may be seriously magnified and become considerably more potent and seemingly disproportionate issues when related to aviation. For that reason, it's imperative to approach some of these issues differently, engaging them from the perspective of their impact on aeromedical decision-making.

Glare/haloes/haze/starbursts/dim lighting/night vision difficulties: These issues interrelate and were discussed under general excimer complications. However, we must consider that the target population of this procedure is clearly intended to be individuals in the moderate to high myopic range (-2.00 D to -6.00 D) who preoperatively in most cases would not be qualified for entry into pilot training. One must understand that within this myopic population the overall improvement in VA more often than not would be far more desirable, have a far wider range of acceptance, and generally not be overridden by any secondary glare that might be involved.

Glare testing remains elusive in many respects, and often is subjective or based on patient surveys. Glare is clearly regarded as an unacceptable element in the aeromedical environment. Glare sources within the cockpit environment can be additive and ultimately exacerbated by a compromised final refractive window, the cornea. Present studies reveal that 30-50% of post-PRK corneas generally appear "clear" on a slit lamp examination and are symptomatically regarded as "clear" during the first year, with a gradual tendency toward clearing over time in most cases. Seiler reports glare and haloes in some post-PRK patients despite clear corneas (6). McDonald reported objective corneal haze present in 64% of patients at 1 year (18). One primate study continued to show histological changes that produce glare still present at 18 months (16). There is no question that glare improves postoperatively, but so far, it cannot be stated that it resolves in everyone, either objectively or subjectively.

In one recent study presented at the Summit Excimer Laser User Group Symposium, 51% of PRK patients (myopes preoperatively less than -6.00 D) complained of glare-disturbed night vision 3 months postoperatively, compared to 14% preoperatively; 12% were regarded to have significant problems driving at night (24). At 12 months, 38% complained of minor disturbances of night vision and 5% significant problems. One alarming study assessed post-PRK disturbances in night vision to be present in 78% of its patients early on, 70% at 1 year, and, and 2 years, 10% complained sufficiently enough of glare that they declined to have PRK performed on the other eye (12). The etiology of glare and haloes, besides histological changes, includes a double pupil effect, the sudden contour ridge between normal tissue and ablated tissue, optical effects from paracentral/corneal islands, and an overall reduction in

contrast sensitivity following this procedure. The double pupil effect is a combination of changing pupil size relative to PRK plateau size and optical changes pro-duced by the abrupt vertical edge at the termination of the PRK zone. Under dimly lit or night tasking, these factors combine to produce glare, haloes and starbursts, all of which impact performance (1,25). Gimbel reports patient survey data revealing that 60% of bilateral PRK patients reported reduced quality of vision in dim light, 38% reduced vision in artifical versus daylight, and 50% reported night driving difficulties (28). Data collected on glare and haze has been variably and subjectively influenced by the assessment techniques employed. Many studies report only haze greater than trace. Kim et al. (1) reported subjective night vision symptoms in 21% and glare/haloes in 10% at 1 year post-PRK. McDonald's (18) data has been interpreted clinically by some to have "virtually all clear corneas" at 6 months. However, 89% of those corneas actually were objectively graded to have trace (barely perceptible haze apparent only to trained observers) or 1+ corneal haze (mild haze not affecting refraction). The correlation between corneal clarity and its impact needs to be further refined. Other studies report the levels of glare/haloes at 1 year were greater than trace in 50% of patients following PRK. Within the general population, trace or less glare may be acceptable, given the uncorrected alternative in myopia, but within the aviation community, unnecessary glare can only be a negative factor exacerbated by the other glare sources inherent in that environment.

Reduced contrast sensitivity: Both induced glare and corneal haze would be expected to reduce the overall contrast sensitivity of the eye. VA standards are based on high-contrast Snellen targets. Under lesser contrast conditions, visual function is determined by contrast sensitivity, which becomes a critical element of performance in the multicontrast aviation environment. Although most countries have no current aviation standards with respect to contrast sensitivity, an individual's ability to perceive contrast has been recognized as a critical element in overall visual performance. A procedure with the potential to negatively impact on contrast sensitivity must be carefully evaluated and monitored until suitable scientific work documents its impact.

Sophisticated contrast sensitivity testing post-PRK is lacking. However, using the Vistech contrast sensitivity chart, an overall compromise in contrast sensitivity across all wavelengths which has persisted up to 1 year has been reported in 1 study in 100% of patients post-PRK (25). Although it can be expected that as haze within the cornea recovers, contrast sensitivity performance will also improve, this question has yet to be resolved and remains a potentially significant issue germane to the aeromedical environment, one requiring a determination to be made after longer follow-up. To do so prematurely or to accept ill-defined reduced contrast sensitivity performance in prospective aviators, until it is fully understood, seems to be a compromise in rational aeromedical logic.

Structural integrity/Stability of refraction: There is no question that RK structurally weakens the eye. This weakness occurs by virtue of the fact that nearly 90% through-and-through incisions are made deliberately in the cornea with a surgical knife. PRK removes a thickness of tissue upwards of 10% of the total corneal depth, within a 6-7 mm zone at the corneal apex. Thus, the overall corneal thickness in any individual is reduced by an amount depending upon the intended refractive impact. Although it appears that any structural weakening of the eye induced by PRK, by virtue of the reduction in thickness and the unknown contribution of Bowman's layer to the cornea, would be expected to be much less than in RK, one cannot predict exactly what the corneal rigidity will be post-PRK. Statements regarding corneal rigidity or strength, without definitive studies to support those claims, cannot be made. It is anticipated that this will not be a clinically significant issue and that there is a possibility that the procedure might "weld" the cornea into a stronger structure. The point is, we do not know yet exactly what occurs post-PRK.

There is a hyperopic shift post-PRK and a period of instability that slows over a 3- to 6-month period, continuing at least 1 year and sometimes beyond. Studies have revealed that refractions may continue to be unstable for up to 26 months (19). This was initially thought to be the case with RK, but we have learned that these refractions can remain unstable for periods of 3-5 years, and new data has shown that RK corneas are susceptible to altitudinal-induced refractive changes. Although the surgical mechanism is different in these two procedures, we cannot predict what the aviation environment's impact will be on post-PRK corneas. This determination awaits further investigation.

Epithelial/subepithelial integrity: We know that the corneal epithelium regenerates and that this tissue normally reattaches to a basement membrane and Bowman's layer of the cornea. PRK, however, removes the normal Bowman's layer and basement membrane over the central cornea, forcing the epithelium to reepithelialize over anterior corneal stroma. At this interface, fine collagen synthesis occurs as well as the formation of new basement membrane material somewhat histologically different from the original. Bowman's layer does not reform. The regenerated epithelial-stromal interface is hyperplastic and associated with increased fibroblastic activity which contributes to this collagen synthesis. The reformation of the basement membrane reveals areas of discontinuity. The presence of Type III collagen has been confirmed in primates by immunofluorescence techniques (26). The long-term sequelae of this new histological alteration of the cornea and the capacity of the epithelium to remain attached to the underlying tissue remains poorly defined. Recurrent erosions or loss of new regenerated corneal epithelium because of ineffective connections with underlying tissue were anticipated to be a more significant problem than has been the case so far. Several recent observations have reasserted concerns over recurrent erosions, but short-term experience is encouraging. Epstein's et al, (19) observations have forced us to redefine corneal stromal remodeling and its time course post-PRK.

Aeromedically, the ability of this altered cornea to support the use of a contact lens has operational significance that will be discussed below.

Endothelial cell layer: The single cuboidal layer of endothelial cells on the innermost surface of the cornea serves as an osmotic pump to remove fluid hydrostatically pushed into the cornea. The endothelial cell population is fixed; these cells lack ability to regenerate. In the presence of increased fluid, the cornea swells and turns opaque; hence, without the endothelium, the cornea would not be able to remain translucent and becomes edematous. Failure of this layer to maintain a clear cornea ultimately leads to the decompensation of the cornea in many disease states causing decreased VA and a potential requirement for corneal transplantation. PRK and its impact on the health of the endothelial cell layers postoperatively, is of concern. So far, there appears to be no recordable loss of endothelial cells, although in some animal studies, there has been a recoverable transient disruption of endothelial cell density over 1 year (27). The production of electron-dense granular material at this layer has been demonstrated in certain animal studies and has raised the question regarding the etiology of this phenomenon and its relationship to PRK (14). There does not seem to be the problem with the endothelium that was anticipated; however, longer-term follow-up in these patients is required to determine the clinical significance of the effects of PRK on this cell layer beyond our limited experience.

Contact lens wear: Because of the aeromedical adoption of contact lenses operationally in some countries for optimal correction of refractive errors (or as an integral part to enhance biological coupling with a weapons system), the post-PRK contact lens issue is a significant one in aircrew. Recognizing that generally 58-75% of the patients are reported to be 20/20 or better uncorrected postoperatively, with 85-95% at 20/40 or better uncorrected, there is still no question that a considerable amount of residual refractive errors will persist and require correction, either by glasses or contact lenses. Even though approximately 75% of the patients are reported so far to have postoperative refractions within $\pm$1.00 D of emmetropia, it appears that 40% of individuals postoperatively will still require correction to assure BVA. In the general population, the importance of this issue is diminished, but aeromedically, it is quite significant. If operationally some countries continue to use contact lenses in aircrew, the health of the corneal epithelium and its capacity to support the use of a contact lens requires serious consideration and evaluation before we assume that aircrew will be able to tolerate these lenses at all following PRK. To date, there is limited clinical experience with soft contact lenses post-PRK. Anecdotally, clinicians involved in PRK studies have found very little requirement to prescribe soft contact lenses in their patients post-PRK. Simply, they are just not being asked for by patients post-PRK. Whether this means the general public is content to have residual uncorrected post-PRK refractive errors because they recognize such a tremendous improvement that any subjective VA disturbance remaining is trivial, or whether glasses suffice, or

neither, remains to be defined before any decision is made with respect to PRK in aircrew who may operationally require contact lenses. Will post-PRK eyes wearing contact lenses be at any increased risk for corneal ulceration or complications because of the alteration in the histological relationship of the cornea post-RK? Will they be able to tolerate contact lenses as long and under the same conditions that have scientifically validated their operational use only after exhaustive clinical research and experience? Additional extensive aeromedical research to justify the use of contact lenses following PRK will be mandatory for those of us who continue to embrace flying candidates with refractive errors, some of whom will certainly pursue PRK privately, or even if at some point we employ PRK for whatever reason aeromedically.

Masking myopic retinopathy: It can be anticipated, just as with orthokeratology and RK in the past, that individuals, in their quest for expensive military aviation training, even in countries with strict entry criteria, will fail to notify the medical screening authorities that they have undergone PRK. In fact, without corneal topography, it will be extremely difficult, if not impossible, to detect individuals who have had this procedure done. These same individuals would have been in the moderate to high myopic category, and not usually within a range of consideration for flying training, even in countries with lenient refractive standards. In general, this range of myopia is at higher risk to develop myopic degenerative retinal changes. It can be anticipated that dilated fundus exams in such cases might not be accomplished according to the otherwise normal routines recommended in such myopes. This could lead to an inability to detect early myopic changes such as tears or holes that might have been identified and treated earlier and puts at risk the considerable financial investment made in what was perceived to be a normal candidate. It would be foolish to assume that everyone who has had this procedure will self-identify during the application process. Corneal topography becomes an essential tool to identify PRK corneas.

Double pupil effect: Seiler reported that more than 10% of patients treated with a 5-mm ablation zone report haloes during night lighting conditions and that glare and haloes also occur in eyes with virtually clear corneas. Even at 2 years, there can be significant glare-induced visual deficits in eyes corrected by more than -6.00 D (6). Although many factors contribute to this night vision problem, the induced double pupil plays a role under dim lighting. By creating a central 6- to 7-mm plateau on the corneal surface, there is the potential to create a situation at the edge of this zone which optically comes into conflict with the dilating pupil under reduced light conditions. This sudden contour cutoff results in optical distortion that will be aggravated by a changing pupillary aperture, creating retinal image degradation, resulting in glare, blurring and visual confusion. Other paracentral corneal effects due to beam heterogeneity (corneal islands) contribute to this phenomenon. Night operations in a high-threat environment make the cockpit a unique environment. This issue is fundamentally different and has significantly

less relevance in the general population, even though within that population we do see problems driving at night (in one study, 10% of the eyes experiencing glare chose not to have PRK on the second eye). No single issue deserves more attention with respect to the aeromedical implications of PRK than the issue of night vision difficulties. Certainly, technological improvements in the future, in both equipment and algorithms, will likely improve on this phenomenon. However, since it is a multidimensional problem, it is anticipated that there will still be considerable potential to compromise night vision. Given that functional clinical tests are less than desirable in assessing this performance category, and given that the nighttime arena will undoubtedly remain supreme, at least initially in any future contingency, then the night vision effects of PRK should loom large in our decision-making process.

Mutagenic/carcinogenic/cataractogenic potential: The same mutagenic/carcinogenic/cataractogenic issues associated with UVC energy levels apply to both civilian and military populations. We cannot begin to predict what the ultimate impact of this radiation will be on the corneal tissue with respect to future scarring and/or the development of metaplastic or neoplastic changes. This is a completely artificial situation, because normally we are not exposed to UVC, even within operational high-altitude environments in or out of the cockpit. We do know that the energy levels associated with the excimer laser are quite high (6.4 eV) and are intended to break chemical and biological bonds within the target tissues to achieve its effect. Unfortunately, it also results in the formation of free radical byproducts--the tissue "bad guys." The association between free radical formation and tumorigenesis is well known. The association of cataracts and UV is also well known. The role of free radical fighters present in the anterior corneal epithelium and their ability to overcome this induced UVC threat is unknown. Will there be an epidemic of cataracts in aircrew 5 or 10 years down the road? Or worse? Are we willing to take this chance in aircrew based on what we know so far? The long-term aftermath and sequelae from this procedure with respect to these issues remains unknown and undoubtedly will do so for decades.

Unknown long-term complications: This issue involves a combination of unpredictable and unforeseeable variables. We do not know what the long-term ramifications of the removal of Bowman's layer to the central cornea will be. We do not know what the long-term consequences of the collagen formation of the type that occurs in response to PRK will be. We do not know if the corneal endothelial cells or any corneal layer will undergo later degenerative changes based on the impact of this procedure. Given the mutagenic/carcinogenic potential of UV radiation in this range, we can only theorize about the long-term consequences of the energy directly applied to the eye. We do not know if UVC, administered in this way, will have any greater impact on cataract formation in the lens. We do not know if any residual corneal haze or scar will worsen in the future, result in changing refractive errors, induced astigmatism or a host of other potentially vision-

debilitating conditions. We do not know what the consequences of all these factors, taken in total, will be on an eye. What we do know is that the 1-year stability issue has been challenged by longer observation.

IV. CONCLUSION

We can all peer into our crystal balls, touch our lucky rabbit's foot, and be optimistically predisposed by the potential significance of this exciting new procedure that makes favorable predictions easy to come by, but we also must recognize that there is a vast difference between acceptability of this procedure in the general population versus the aeromedical community. One can even get up on a soapbox and herald warnings of pending ocular doom. The fact is, none of that is science.

Assessment of PRK and its issues obviously will take many years, and during that time caution should be the byword. Despite the relative inexperience with this procedure and the data presented based on only a few years of observation, there appears to be no question that PRK will provide myopes with an available alternative to glasses and contact lenses. PRK will undoubtedly become routine, proven technology, providing that unacceptable complications do not arise. However, the applicability of PRK to prospective aviation candidates and exquisitely trained assets is an entirely different matter. I can find no medical rationale supporting a procedure's application to a potential aviation candidate pool while it is still clinically evolving and aeromedically unnecessary. It must be remembered that we should approach aviation candidates from the perspective of a long-term investment. They are expensive and important resources who are becoming even more critical as our air forces drawdown. (Hopefully, they will not become an endangered species!) No one can forecast whether an individual who has received a PRK is a good candidate for graduation from flying training, let alone provide a return on the tremendous financial investment made in that individual. What little is known and the vast majority of what is still unknown about this procedure should dictate that medical and fiscal prudence be the rule. I do not believe that, as aerovisual scientists, we should aggressively challenge our standards with a new and unknown area of science, circumventing sound medical judgment, and allow these individuals to fly. If we are interested in selecting the best possible candidates, given the realities of the diminished training allocations, there appears to be no need to consider a procedure and all of its ramifications and potential problems in our specialized population. It makes more profound sense to approach this procedure conservatively from the sidelines, to analyze it with respect to our unique medical environment, and to make an informed but highly specialized decision only after we have satisfied ourselves that the procedure is absolutely safe and, hopefully, predictable. In the meantime, we should advocate for a unanimity of opinion against the appropriateness of this procedure in aircrew. Any endorsement less than this is a Pandora's Box that, once opened, will be difficult to close, on sheer inertia, as vast numbers of individuals receive PRK in the future and challenge our standards. If we do it for one, what stops us

from doing it for all? Until further issues evolve, we should maintain a diligent watch but continue to regard PRK as disqualifying for flying.

PRK truly warrants recognition for its outstanding technological contribution to ophthalmology and many accolades are deserved by those visionaries who developed it. However, I draw the line, at least for the moment, in its applicability to aircrew. Personally, I hope the procedure continues to evolve and becomes the ultimate solution to myopia, because I have a son with -2.00 D of myopia who wants to be a USAF fighter pilot!

I will end with a phrase that appears in some form at the conclusion of many of the studies and papers published on PRK: "The accuracy of a single treatment of PRK is acceptable and stable over a short-term. Longer-term follow-up, however, is needed to assess the stability of the result over multiple years" (30).

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